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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,373	09/22/2003	Hidehiro Yamazaki	033025-006	5015

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EXAMINER	
PAK, JOHN D	

ART UNIT	PAPER NUMBER
1616	

NOTIFICATION DATE	DELIVERY MODE
02/24/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/665,373	YAMAZAKI, HIDEHIRO	
	Examiner	Art Unit	
	John Pak	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-8 and 10-16* is/are pending in the application.

4a) Of the above claim(s) *5-8,10-14 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1, 3-8, 10-16 are pending in this application. Claims 5-8, 10-14 and 16 remain withdrawn as being directed to non-elected subject matter. Claims **1, 3-4,** and **15** will presently be examined to the extent that they read on the elected subject matter.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-4 and 15 stand rejected under 35 U.S.C. 103(a) as being unpatentable over JP 10-203961 in view of Medline abstract 93060291, Shozo et al. (1986), HCAPLUS abstract 1984:188290 and HCAPLUS abstract 1997:400035.

JP 10-203961[1] discloses treating ketoacidosis, without causing alkalosis, by administering a solution that contains the following electrolytes:

	Range	Preferred range
sodium:	120-150 mEq/L	125-145 mEq/L
potassium:	0-10 mEq/L	0-5 mEq/L
chloride :	90-120 mEq/L	95-115 mEq/L
calcium :	0-5 mEq/L	1-4 mEq/L
magnesium:	0-5 mEq/L	1-4 mEq/L
bicarbonate:	20-35 mEq/L	22-33 mEq/L
citrate:	1-5 mEq/L	1-4 mEq/L.

See translation of claim 1 and paragraphs 5, 7-9. Correction of acidosis with bicarbonate is generally disclosed (translation of paragraphs 2-3). The electrolyte

[1] This is a Japanese language document. For applicant's convenience, a full English (human) translation is provided herewith. All discussion and reference are to this translation, not the previous (machine) translation provided in previous Office actions.

solution set forth above is administered as an infusion for "surgical invasion, and the like" to supply electrolytes in a balanced manner (translation of paragraph 13). Correcting decrease of arterial blood pH is taught (translation of paragraph 14). Dose is taught to be suitably adjusted according to a patient's symptoms, age, weight, etc., at 500-8000 ml/per day (id.).

Medline abstract 93060291 discloses that hormonal change after surgical stress and anaerobic glucolysis due to tissue ischemia cause acidosis. Postoperative complications also cause acidosis. Acidosis is specifically found in gastrointestinal surgery. Alkalosis is discussed as a result of bicarbonate production from lactate and citrate supplied by massive infusion and transfusion.

Shozo et al. (submitted by applicant with the IDS of 2/3/2004) disclose the various technological considerations involved in administering sodium bicarbonate in fluid therapy (see entire English translation submitted by applicant). Section 3 of the article (translation pages 3-4) discloses that sodium bicarbonate administration speed and quantity for treating metabolic acidosis are known. Maximum speed is 100 mEq/hour and a formula is given for administration quantity, which are adjusted for condition of the patient (id.).

HCAPLUS abstract 1984:188290 discloses that the use of blood gas analytical parameters for monitoring and therapy of patients with acid-base disturbances is known.

HCAPLUS abstract 1997:400035 discloses an apparatus capable of determining CO_2 partial gas pressure and pH from blood gas analysis for clinical diagnosis. The apparatus is "convenient for monitoring acidosis or alkalosis."

Controlling electrolyte balance is explicitly taught by JP 10-203961, and controlling water balance would be obtained from the administration of the same exact solution. The patient in JP 10-203961 suffers from ketoacidosis, which is a type of metabolic acidosis, **and can include patients undergoing surgery**. The makeup of the preferred solution in JP 10-203961 compares as follows with applicant's invention:

	JP 10-203961	Applicant's claimed invention
sodium:	122-145 mEq/L	130-145 mEq/L
potassium:	0-5 mEq/L	2-5 mEq/L
chloride :	95-115 mEq/L	90-130 mEq/L
calcium :	1-4 mEq/L	2-5 mEq/L
magnesium:	1-4 mEq/L	0.5-2.5 mEq/L
bicarbonate:	22-33 mEq/L	20-35 mEq/L
citrate:	1-4 mEq/L	1-7 mEq/L.

It is the Examiner's position that the concentration of the claimed invention would have been fairly suggested to the ordinary skilled artisan in this field from the narrow range of identical components disclosed by JP 10-203961. Even if it could be argued that the solution in JP 10-203961 does not match exactly in content, one having ordinary skill in the art would have been motivated to adjust from the narrow range taught by JP 10-203961 the solution makeup and concentration as claimed to control water and electrolyte balance and acid-base equilibrium in patients suffering from metabolic acidosis and surgical or postoperative patient. The motivation for such adjustment would come from monitoring and responding to the patient's blood parameters, which must be done when treating acid imbalance.

As for the claimed feature of 5-20 ml/kg/hour, the Examiner's position is that such infusion speed is fairly suggested by the prior art taken as a whole. Shozo et al. disclose "criterion for calculating … administration speed and administration quantity is

established" (translation page 3, last full paragraph). 100 mEq/hour is the *maximum* speed of infusion, wherein flexibility is taught depending on condition of a patient and "[s]lower administration speed in general is enough" (translation page 4, lines 2-3). For comparison, applicant's 5-20 ml/kg/hr is equivalent to:

6-42 mEq bicarbonate/hour for a 60 kg person,

8-56 mEq/hr for a 80 kg person,

10-70 mEq/hr for a 100 kg person, and

14-84 mEq/hr for a 120 kg person.

To the ordinary skilled artisan, the claimed 5-20 ml/kg/hour feature would thus have been obvious from the combined teachings of the prior art since determining how much of the infusion to administer or how fast to administer would depend on patient condition and weight, with the proviso that the ultimate bicarbonate administration speed is no higher than the established rate of 100 mEq/hr.

The secondary references HCAPLUS abstract 1984:188290 and HCAPLUS abstract 1997:400035 further establish the motivation of the ordinary skilled artisan to adjust the infusion speed or demedication of the solution as necessary, because said references establish that close monitoring of the patient's blood parameters via blood gas analysis is practiced when treating acidosis. The secondary reference by Medline abstract further establishes the motivation of ordinary skilled artisan to treat surgical and postoperative patients with the solution taught by JP 10-203961.

As for the feature of claim 3, which requires adjusting infusion speed to maintain a plasma bicarbonate concentration to be in a range of 22 to 26 mEq/L, such step would

have been obvious for returning the patient's blood profile to normal levels since the normal plasma bicarbonate concentration in humans is 24 mEq/L.

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly disclosed or suggested by the teachings of the cited references.

Applicant's remarks relative hereto, filed on 11/13/2008, have been given due consideration but they were deemed unpersuasive.

Applicant argues that the preparation of JP 10-203961 is used for a patient with diabetes, whereas the present invention relates to a patient undergoing an operation or a postoperative patient. This argument is unpersuasive because JP 10-203961 discloses its preparation for "diabetes, **surgical invasion**, and the like" to supply electrolytes in a balanced manner (translation of paragraph 13, emphasis added). Applicant's argument is additionally unpersuasive because the claimed "patient undergoing an operation" or "postoperative patient" fails to exclude a diabetic patient. Diabetic patients encounter surgical invasion as their condition worsens and It is known from Medline abstract 93060291 that postoperative complications cause acidosis. Administration to a patient within the scope of applicant's claim language is fairly suggested.

Applicant further argues that the prior art does not teach or suggest the specific rate of infusion speed by observing a data of blood gas analysis as an index parameter

of the present invention. This argument is also unpersuasive because the prior art is amply suggestive of the same.

The same electrolyte infusion is known for treating acidosis, ketoacidosis (JP10-203961) to “supply electrolytes in a balanced manner" (translation of paragraph 13). "The dosage of the electrolyte infusion ... can be adjusted as appropriate according to the condition, age, weight, and so forth of the patients ….” (id.). “Correcting the decrease of arterial blood pH **without causing alkalosis**" is disclosed (translation of paragraph 14). Shozo et al. disclose the level of ordinary skill in the art in being able to take into account various technological considerations and patient condition to arrive at administration speed and adjustment thereof; and the two HCAPLUS abstracts clearly teach the use of blood gas analytical parameters for monitoring the therapy of patients with acidosis. pH, pCO_2, pO_2 and [$HCO3^+$], as well as concentration of other electrolytes are all obtainable from blood gas analysis (HCAPLUS abstract 1997:400035), and such data would inform the ordinary skilled artisan of the patient's water and electrolyte balance, as well as acid-base equilibrium, because such data are all interrelated with respect to water, electrolyte concentration and acidity. Such information would obviously convey the progress of the therapy in treating the patient’s acidosis such that one of ordinary skill in the art would be capable and motivated to use such feedback to adjust infusion speed and/or quantity.

Applicant also argues the advantage of acidosis treatment without inducing metabolic alkalosis during infusion and alkalosis after stopping treatment, without causing problems of hypernatremia. However, JP 10-203961 expressly teaches

acidosis treatment without alkalosis, and the sodium concentration of applicant's solution (130-145 mEq/L) is very close to that of JP 10-203961's preferred solution (122-145 mEq/L). Hence, if hypernatremia is avoided during acidosis treatment in applicant's invention, the same would be obtained in the prior art acidosis treatment that has the same or lower sodium concentration.

For these reasons, applicant's arguments fail to take full account of the combined teachings of the prior art as a whole, and such arguments have been found unpersuasive. All claims must be rejected again.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to John Pak whose telephone number is **(571)272-0620.** The Examiner can normally be reached on Monday to Friday from 8 AM to 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's SPE, Johann Richter, can be reached on **(571)272-0646**.

The fax phone number for the organization where this application or proceeding is assigned is **(571)273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/John Pak/
Primary Examiner, Art Unit 1616